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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/785,215	02/20/2001	Martin Roland Jensen	3631-0107P	7660

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EXAMINER
NICHOLS, CHRISTOPHER J

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 12/19/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/785,215	JENSEN ET AL.	
	Examiner	Art Unit	
	Christopher Nichols, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21.10.2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29,33 and 59-67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-29,33, and 59-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-29,33 and 59-67* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 February 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election **without** traverse of Group I (Claims 1-29 and 33) with the addition of claims 59-67, in part drawn to a method for *in vivo* down-regulation of amyloid protein in an animal, wherein presentation of an amyloidogenic polypeptide to the immune system is effected by introducing the amyloidogenic polypeptide or its analogue into the animal cell in Paper No. 10 (24 October 2002) is acknowledged. Claims 30-32 and 34-58 are cancelled.

Status of Application, Amendments, and/or Claims

2. The Preliminary Amendment in Paper No. 4 (4 January 2001) has been entered in full. The Preliminary Amendment in Paper No. 10 (24 October 2002) has been entered in full. Claims 30-32 and 34-58 are canceled. Claims 59-67 have been added. Claims 1-29, 33, and 59-67 are under examination.

3. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1647, Examiner Christopher Nichols.

Priority

4. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Panama on 21 February 2000. It is noted, however, that applicant has not filed a certified copy of the PANAMA 2000 00265 application as required by 35 U.S.C. 119(b).

5. The effective US filing date for this application is 1 March 2000 based on applicant's claim for domestic priority under 35 U.S.C. 119(e) to the provisional application (60/186295) filed on 1 March 2000.

Oath/Declaration

6. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

> The oath or declaration is defective because: incorrect application number is cited "009/785215". The correct application number is "09/785215".

Specification

7. The Specification is objected to because of the following informalities: The disclosure's discussion of the figure should be entitled: "Brief Description of Figure" (pp. 17); sentence does not end in a period (pp. 25 line 18, pp. 61 line 31); "structure" is misspelled (pp. 49 line 7). Appropriate correction is required.

Claim Objections

8. Claims 1-29, 33, and 59-67 are objected to because of the following informalities: the claims recite non-elected material. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-29, 33, and 59-67 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

10. Claim 1 is directed to a method for in vivo down-regulation of amyloid protein in an animal. Claim 2 is directed to the method according to claim 1, wherein an analogue of SEQ ID NO: 2 with at least one modification of the amino acid sequence. Claim 3 is directed to the method according to claim 2, wherein the modification has a result that a substantial fraction of B-cell epitopes of the amyloidogenic polypeptide is preserved. Claim 4 is directed to the method according to claim 3, wherein the modification includes introduction of side groups. Claim 5 is directed to the method according to claim 3, wherein the modification includes amino acid substitution, deletion, insertion, and/or addition. Claim 6 is directed to the method according to claim 5, wherein the modification results in the provision of a fusion polypeptide. Claim 7 is directed to the method according to claim 5, wherein introduction of the amino acid substitution, deletion, insertion, and/or addition results in a substantial preservation of the overall tertiary structure of the amyloidogenic polypeptide. Claim 8 is directed to the method of claim 2, wherein the modification includes duplication of a least one B-cell epitope and/or introduction of a hapten. Claim 9 is directed to the method according to claim 3, wherein the foreign T-cell

epitope is immunodominant in the animal. Claim 10 is directed to the method of claim 3, wherein the foreign T-cell epitope is promiscuous. Claim 11 is directed to the method according to claim 10, wherein the natural T-cell epitope is a diphtheria toxoid epitope. Claim 12 is directed to the method according to claim 3, where the first moiety is a specific binding partner. Claim 13 is directed to the method of claim 3, wherein the second moiety is HSP70. Claim 14 is directed to the method according to claim 3, wherein the third moiety is a polyhydroxypolymer. Claim 15 is directed to the method according to claim 65, wherein the polysaccharide serves as a carrier backbone to which the amloidogenic polypeptide and the foreign T-cell epitope are separately bound. Claim 16 is directed to the method according to claim 15, wherein the amyloidogenic polypeptide and the foreign T-cell epitope are bound via an amide bond to the polysaccharide. Claim 17 is directed to the method according to claim 1, wherein the amyloidogenic polypeptide has been modified so as to preserve B-cell epitopes. Claim 18 is directed to the method according to claim 17, wherein the amyloidogenic polypeptide has been modified so as to lack at least one B-cell epitope. Claim 19 is directed to the method according to claim 1 which comprises a substitution of at least one amino acid sequence within the amyloidogenic polypeptide. Claim 20 is directed to the method according to claim 1 wherein the amyloidogenic polypeptide is beta-amyloid (Aβ, SEQ ID NO: 2). Claim 21 is directed to the method according to claim 1, wherein the amyloidogenic polypeptide is Aβ. Claim 22 is directed to the method according to claim 21, wherein the amino acid sequence containing the foreign T_H epitope is introduced into the amyloidogenic polypeptide. Claim 23 is directed to the method according to claim 22, wherein the amyloidogenic polypeptide comprises amino acid residues 672-714 of SEQ ID NO: 2. Claim 24 is directed to the method according to claim 23, wherein

the amyloidogenic polypeptide comprising the amino acid sequence of amino acid residues 672-714 of SEQ ID NO: 2. Claim 25 is directed to the method according to claim 1, wherein presentation to the immune system is effected by having at least two copies of the amyloidogenic polypeptide. Claim 26 is directed to the method according to claim 1, wherein the amyloidogenic polypeptide has been formulated with an adjuvant. Claim 27 is directed to the method according to claim 1, wherein an effective amount of the amyloidogenic polypeptide is administered to the animal. Claim 28 is directed to the method according to claim 27, wherein the effective amount is between 0.5 μg and 2,000 μg. Claim 29 is directed to the method according to claim 27, wherein the amyloidogenic polypeptide is contained in a virtual lymph node (VLN) device. Claim 33 is directed to the method according to claim 22, including at least one administration a year. Claim 59 is directed to the method according to claim10, wherein the foreign T-cell epitope is selected from a natural promiscuous T-cell epitope and an artificial MHC-II binding peptide sequence. Claim 60 is directed to the method according to claim 11, wherein the tetanus epitope is P2 (SEQ ID NO: 4). Claim 61 is directed to the method according to claim 12 wherein the specific binding partner is selected from a hapten and a carbohydrate for which there is a receptor on the B-lymphocyte or the APC. Claim 62 is directed to the method according to claim 13, wherein the cytokine is selected form a group. Claim 63 is directed to the method according to claim 13, wherein the heat shock protein is Hsp70. Claim 64 is directed to the method according to claim 14, wherein the third moiety is a palmitoyl group. Claim 65 is directed to the method of claim 14, wherein the polyhydroxypolymer is a polysaccharide. Claim 66 is directed to the method according to claim 33 comprising at least 2 administrations per year. Claim 67 is directed to the method according to claim 66, comprising at least 3 administrations per year.

11. The specification teaches that mice transgenic for human APP (TgRND8+) express a mutated form of APP that results in high concentration of Aβ-40 and Aβ-42 is their brains. These mice were immunized with 100 mg of Aβ-42 (SEQ ID NO: 673-714) or 50 mg of HAβ43+-34 variant construct four times at two-week intervals. The mice produced antibodies in response to these immunizations.

12. The art teaches that the administration of particular $A\beta_{42}$ (AN1792) fragments in with an immunogenic adjuvant is able to reduce β-amyloid levels within the brains of mice that are transgenic for PDAPP. These mice exhibit Alzheimer type over production and build up of β - amyloid within the brain. However, as recognized in the art, these mice do not exhibit Alzheimer's disease as in humans or plaque morphology and components which are the same as in humans, Alzheimer's disease, Down's Syndrome or other amyloidogenic diseases, see in particular Schenk et al., Nature, 400:173-77, 1999, Games et al., Nature 373(6514): 523-7, 1995 and Chen et al., Progress in Br. Res., 117:327-34, 1998.

13. Furthermore, the method is based upon findings that show particular strategies of targeting plaque removal via antigen or antibody administration. Evidence that such therapy can be effective in the removal of amyloid plaque burden is exhibited by Lemere et al., Society for Neuroscience Abstracts, vol. 25, part I, Abstract 519.6, 29th Annual Meeting 10/23-10/28, 1999, and Schenk, Nature, 400:173-177, (1999) using antigen and DeMattos, PNAS 98(15): 8850-8855, 2001 using antibody administration (Raso, V.A., Immunotherapy Weekly, Abstract "Immunotherapy of Alzheimer's Disease", (1998).

14. While general guidance is given in the specification on the use of a fragment of SEQ ID NO: 2 (residues 672-714) to make antibodies, no working examples are given re: vaccination of

subjects using the SEQ ID NO: 2 fragment, other fragments of SEQ ID NO: 2, analogues of SEQ ID NO: 2 or the 672-714 fragment, or a specific immune response elicited by the SEQ ID NO: 2 fragment which leads to an *in vivo* down-regulation of amyloid protein.

15. Thus the claimed invention is directed using Aβ peptide to produce an in vivo down-regulation of amyloid protein in an animal, which is not supported by the teachings of the specification or the prior art (Tennent et al., 1995; Stein and Johnson, 2002). One skilled in this art would be expected to reasonably doubt that the claimed method would work due to the following obstacles: Specific biological actions/activities that the antigenic composition of Aβ peptide and an adjuvant would effect; How does the immunogenic effect on amyloid deposition relate to symptoms of amyloid-related diseases; Expectation of that Aβ peptide would be actively involved in amyloid deposition, as opposed to being a non-dynamic component (USPT 5851996; USPT 5780587; Perutz et al., 2002); the effects of an immune response to an antigen. The specification does not provide guidance on how to overcome expected obstacles. The scope of patent protection sought by Applicant as defined by the claims fails to correlate reasonably with the scope of enabling disclosure provided by the specification and prior art for the following reasons.

16. Regarding immune response, the art recognizes that immune responses include two large branches, humoral and cellular. Due to the large quantity of experimentation necessary to evaluate all the possible aspects of both humoral and cellular immune responses, the lack of direction/guidance presented in the specification which aspects of the immune response are most relevant, the absence of working examples directed to all aspects of immune responses, the complex nature of the invention, the unpredictability of the effects of antigens on the mammalian

immune system (Chapman, 2000; Frenkel et al., 1999; Frenkel et al., 1998; Frenkel et al., 2000; Friedland et al., 1997), and the breadth of the claims which fail to recite limitations for which aspects of a mammalian immune response are activated, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

17. Regarding the ancillary effects of the introduction of an immune response in a mammalian nervous system, the specification must establish that the antigens injection into the subjects produce a specific immune response and do not act as pyrogens (leading to cranial swelling for example). Due to the large quantity of experimentation necessary to evaluate all the effects of the difficulty of predicating an immune response in the nervous system, the lack of direction/guidance presented in the specification about collateral damage due to a vigorous immune response in an immunological privileged area (such as the nervous system), the absence of working examples directed to successful antigen presentation of a neurological protein, the complex nature of the invention, the unpredictability of the effects of antigens on the mammalian nervous system, and the breadth of the claims which fail to recite limitations for what constitutes a successful, controlled immune response in the mammalian brain, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope (Elan press releases; Grubeck-Loebenstein et al., 2000; USPN 598883).

18. Regarding, mutants, fragments, and peptides, the skilled artisan readily recognizes that protein chemistry is an unpredictable area of biotechnology. Proteins with replacement of single amino acid residues may lead to both structural and functional changes in biological activity and immunological recognition see in particular Skolnick et al. (2000). For example, Jobling et al. (1991) teaches a panel of single amino acid substitutions by oligonucleotide directed

mutagenesis which produce proteins that differ in native conformation, immunological recognition, binding and toxicity, thus exemplifying the importance of conserved structural components to both biological function and immunological recognition. The skilled artisan also recognizes that immunological responses depend upon the structural characteristics (conformation) of the particular protein (amino acid sequence) targeted.

19. Regarding down-regulation, the art recognizes that down-regulation entails several steps, including but not limited to transcriptional, translation, post-translation modification, recognition, and inhibition (competitive, non-competitive, uncompetitive) and has unpredictable effects on a cell signal function. Due to the large quantity of experimentation necessary to all the applicable kinds of down-regulation, the lack of direction/guidance presented in the specification regarding evaluating effects of the claimed invention on down-regulation, the absence of working examples directed to down-regulation, the complex nature of the invention, the unpredictability of the effects of down-regulation on the amyloid protein (WO 95/05849; WO 02/34777; WO 01/39796), and the breadth of the claims which fail to recite limitations for what constitutes down-regulation, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

20. Regarding analogs, the art recognizes that even minor alterations to protein structure have unpredictable effects on a proteins function, in addition, analogue can pertain to chemical entities and biologically derived substances as well as proteinaceous substances. Due to the large quantity of experimentation necessary to all the applicable analogs of SEQ ID NO: 2 (and specified changes contained in the specification), the lack of direction/guidance presented in the specification regarding synthesizing, screening, and evaluating non-peptide analogs of SEQ ID

NO: 2, the absence of working examples directed to non-peptide analogs of SEQ ID NO: 2, the complex nature of the invention, the unpredictability of the effects of mutation on protein structure and function (Wells, 1990; Murray et al., 1990; Marks, 1989), and the breadth of the claims which fail to recite limitations for what constitutes an analog, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

21. Regarding modification, the art recognizes that modification entails several chemical reactions, including but not limited to addition of chemical entities, removal of chemical entities, genetic mutations, and has unpredictable effects on a cell signaling molecule function. Due to the large quantity of experimentation necessary to all the applicable kinds of modification, the lack of direction/guidance presented in the specification regarding evaluating effects modification of the molecule, the absence of working examples directed to modified molecules, the complex nature of the invention, the unpredictability of the effects of modification on the function of molecules (WO 95/05849; WO 01/39796), and the breadth of the claims which fail to recite limitations for what constitutes modification, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

22. Regarding amino acid substitution, the art recognizes that changing a codon which codes for a particular amino acid includes substitution, deletion, insertion, addition which can result in frame-shift mutations, single amino acid mutations, non-sense mutations, and silent mutations. Due to the large quantity of experimentation necessary to evaluate all the possible effects of mutation on peptide formation, the lack of direction/guidance presented in the specification on what specific mutations in the codons are to be acted upon, the absence of working examples

directed to the effects of all the claimed mutations on the peptide, the complex nature of the invention, the unpredictability of the effects of mutations (Wells, 1990; Murray et al., 1990; Marks, 1989), and the breadth of the claims which fail to recite limitations for what effects mutations would have on peptide formation, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

23. The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an

invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone (Bork, 2000, Genome Research 10:398-400; Skolnick et al., 2000, Trends in Biotech. 18(1): 34-39, especially p. 36 at Box 2; Doerks et al., 1998, Trends in Genetics 14:248-250; Smith et al., 1997, Nature Biotechnology 15:1222-1223; Brenner, 1999, Trends in Genetics 15:132-133; Bork et al., 1996, Trends in Genetics 12:425-427). Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

24. Concerning β-amyloid (Aβ) and fragments thereof, Tanaka et al. (1998) demonstrates that administration of β-amyloid (1-40) into the cerebral ventricle of rats produces learning and memory deficits accompanied by dysfunction in the cholingergic and dopaminergic systems (Abstract). Therefore, instead of eliciting a salubrious immune response to alleviate a β-amyloid

disorder, such as Alzheimer's disease, the administration of the β-amyloid protein or fragments thereof can lead to detrimental neurological effects (Münch and Robinson, 2002).

25. Finally, the application must establish a nexus between the specific immune response recited in the claims and the down-regulation of amyloid protein in an animal recited in the claims. In this case, the skilled artisan is not guided as to how an immune response must affect one or more activates of Aβ such that the immune response would be determined to be one that alleviates a disorder (most likely Alzheimer's disease). Also, amyloid related disorders are varied and it is not clear that Aβ would be sufficiently involved in a rate-limiting step for any amyloid related disorder such that it could be used in a to elicit a specific and sufficient immune response to down-regulate amyloid protein thereby providing relief from an amyloid-related disorder or disease (Zheng et al., 1996; Small et al., 2001; Chapman, 2000; Esiri, 2001; St. George-Hyslop and Westaway, 1999; Younkin, 2001; Tennent et al., 1995; Stein and Johnson, 2002).

26. Claims 1, 11, and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Regarding claim 1, a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not

required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 1 recites the broad recitation "animal", and the claim also recites, "including a human being" which is the narrower statement of the range/limitation.

27. Claim 11 recites the limitation "the natural T-cell epitope" in the second line. There is insufficient antecedent basis for this limitation in the claim.

28. Claim 22 is incomplete as it refers to "FIG 1" for incorporation of limitations.

Summary

29. Claims 1-29, 33, and 59-67 are hereby rejected.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher Nichols, Ph.D. whose telephone number is 703-305-3955. The examiner can normally be reached on Monday through Friday, 8:30AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, Ph.D. can be reached on 703-308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications. The fax phone numbers for the customer service center is 703-872-9305.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Elizabeth C. Kemmerer

CJN
December 12th, 2002

ELIZABETH KEMMERER
PRIMARY EXAMINER